IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:	Confirmation No.: 7102
Philip W. MILLER *et al.*	Art Unit: 1637
Application Serial No.: 09/692,257	Examiner: Joyce Tung
Filed: October 19, 2000	Attorney Docket No.: 16517.297

Title: Nucleic Acid Molecules and Other Molecules Associated with Plants

APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is an Appeal from the Final Rejection of claims in the above-captioned patent application. A Notice of Appeal was filed on February 12, 2007. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter.

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellants identified the following judicial proceeding, which may have a bearing on the Board's decision in the present Appeal. On May 27, 2004, the Real Party in Interest in the above-captioned matter filed an appeal to the United States Court of Appeals for the Federal Circuit ("Federal Circuit") from a decision by the Board in *In re Fisher.* (U.S. Patent Application

Serial No. 09/619,643; BPAI Appeal No. 2002-2046; Federal Circuit Case No. 04-1465). The Federal Circuit's decision in *In re Fisher* may have a bearing on the Board's decision with regard to at least one of the grounds of rejection in the present appeal. A copy of the Board's decision in Appeal No. 2002-2046 and a copy of *In re Fisher*, 412 F.3d 1365 (Fed. Cir. 2005) are attached hereto in the Related Proceedings Appendix.

Appellants filed an Appeal Brief in U.S. Patent Application Serial No. 09/684,016; in U.S. Patent Application Serial No. 10/361,942; in U.S. Patent Application Serial No. 09/199,129; in U.S. Patent Application Serial No. 09/920,953; in U.S. Patent Application Serial No. 09/663,423; in U.S. Patent Application Serial No. 09/237,183; and in U.S. Patent Application Serial No. 10/437,963; which also may have a bearing on the present appeal.

3. Status of Claims

Claims 1 and 8 to 13 are pending. Claims 2 to 7 were cancelled without prejudice by Appellants in the response dated November 14, 2002. Claims 1 and 8 to 13 stand finally rejected under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph. Claims 8 to 13 stand additionally rejected under 35 U.S.C. § 112, first paragraph. Appellants appeal each of the rejections of claims 1 and 8 to 13.

4. Status of Amendments

Appellants have not filed any responses to the final Office Action dated November 13, 2006 ("Final Action").

5. Summary of Claimed Subject Matter

Independent Claim 1: The subject matter of independent claim 1 is directed to a substantially purified nucleic acid molecule that encodes a maize protein comprising a nucleic acid sequence of SEQ ID NO: 1 or its complement. *Specification* at page 9, lines 24 to 26.

Independent Claim 8: The subject matter of independent claim 8 is directed to a substantially purified nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or its complement. *Specification* at page 10, lines 1 to 3.

Independent Claim 10: The subject matter of independent claim 10 is directed to a substantially purified first nucleic acid molecule comprising a fragment from about 50 to about 100 nucleotide residues, wherein said fragment exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and its complement. *Specification* at page 16, lines 20 to 25 and page 18, lines 5 to 27.

Independent Claim 13: The subject matter of independent claim 13 is directed to a substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule, wherein said fragment consists of about 50 to about 100 nucleotide residues of the nucleic acid molecule of SEQ ID NO: 1 or its complement. *Specification* at page 16, lines 20 to 25 and page 18, lines 5 to 27.

A copy of the claims on appeal is attached hereto in the Claims Appendix.

6. Grounds of Rejection to be Reviewed on Appeal

The grounds of rejection to be reviewed in this Appeal are that pending claims 1 and 8 to 13 stand rejected under 35 U.S.C. § 101, because the claimed invention is allegedly not supported by either a specific or substantial utility or a well-established utility; claims 1 and 8 to

13 stand rejected under 35 U.S.C. § 112, first paragraph, because, since the claimed invention is allegedly not supported by either a specific or substantial or a well-established utility, one skilled in the art would not know how to use the claimed invention; and that claim 1 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

7. Argument

A. Summary of Appellants' Position

The specification provides a specific, substantial, and well-established utility for the nucleic acid sequence of SEQ ID NO: 1. Appellants have provided several substantial and well-established utilities for SEQ ID NO: 1, and these utilities are specific, *i.e.*, they are not applicable to any general nucleic acid sequence. In setting forth at least these specific, substantial, and well-established utilities, Appellants have demonstrated that the claimed invention satisfies the requirements of 35 U.S.C. §§ 101 and 112, first paragraph, with respect to claims 1 and 8 to 13. Further, by describing a common structural feature of the claimed nucleic acid molecules, Appellants have satisfied the written description requirement under 35 U.S.C. § 112, first paragraph, with respect to claim 1.

B. The Claimed Nucleic Acids Have Utility under 35 U.S.C. § 101

The Examiner rejected claims 1 and 8 to 13 under 35 U.S.C. § 101, because the claimed invention allegedly "is not supported by either a specific or substantial utility or a well-established utility." Final Action at page 2.

The Examiner admits that the specification discloses many uses for polynucleotides, which include the claimed polynucleotide SEQ ID NO: 1, such as identifying promoters involved

in gene regulation, determining whether a plant contains a mutation, and acting as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function. Final Action at page 2. However, the Examiner considers the disclosed utilities non-specific, applicable to polynucleotides in general, and not specific to the polynucleotide claimed. *Id.* at pages 2-3.

In *In re Fisher*, the Federal Circuit reiterated that the "basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with *substantial utility*." *In re Fisher*, 421 F.3d 1365, 1371 (Fed. Cir. 2005) (citing *Brenner v. Manson*, 383 U.S. at 534-35, 1966) (emphasis in original). The Court noted that since *Brenner* "our predecessor court, the Court of Customs and Patent Appeals, and this court have required a claimed invention to have a specific and substantial utility to satisfy § 101." *Id.* Although the Supreme Court has not defined the meaning of the terms "specific" and "substantial", the Federal Circuit has identified a framework for the kind of disclosure an application could contain to establish a specific and substantial utility. *In re Fisher*, 421 F.3d at 1371. First, the Court indicated that to provide a substantial utility, the specification should disclose a utility such that "one skilled in the art can use a claimed discovery in a manner which provides some *immediate benefit to the public*." *Id.* (emphasis in original). Second, a specific utility can be disclosed by discussing "a use which is not so vague as to be meaningless," that is that the claimed invention "can be used to provide a well-defined and particular benefit to the public." *Id.*

Appellants have asserted throughout the specification that the claimed nucleic acid molecules provide identifiable benefits, for example use to identify the presence or absence of a polymorphism associated with, for example, cold-response genes, and use as a marker of cold

tolerance. *Specification* at page 34, line 21 to page 35, line 8. Either of these utilities described alone is enough to satisfy 35 U.S.C. § 101 because these utilities are neither vague nor impractical. Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown"). In other words, Appellants have established at least one specific, practical utility for the claimed polynucleotides, thereby satisfying the requirements of 35 U.S.C. § 101.

Moreover, these utilities are not applicable to all polynucleotides in general because the claimed polynucleotides are obtained from cold-treated young maize seedlings. *See, for example, Specification* at page 88 (Example 1). Therefore, they have utilities that are specific to them, utilities that are not shared by polynucleotides in general. For example, polymorphisms identified by the claimed nucleotides would not be identified by just any random, general polynucleotide.

The Examiner appears to challenge the credibility of the presently asserted utilities. Utility is determined "by reference to, and a factual analysis of, the disclosure of the application." *In re Ziegler*, 992 F.2d 1197, 1201 (Fed. Cir. 1993), *quoting Cross v. Iizuka*, 753 F.2d 1040, 1044 (Fed. Cir. 1985). The Examiner "has the initial burden of challenging a presumptively correct assertion of utility in the disclosure." *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995). The utilities asserted in the specification must be accepted as factually sound unless the U.S. Patent and Trademark Office cites information that undermines the credibility of the assertion. *Id.* The Examiner "must do more than merely question operability – [she] must set forth factual reasons which would lead one skilled in the art to question the objective truth of

the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1224-25 (C.C.P.A. 1975) (emphasis in the original); M.P.E.P. § 2107 ("Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided ..."). Here, the Examiner has not met this burden.

The Examiner merely states that "there is no statement that SEQ ID NO: 1 is used as a marker of cold tolerance in Example 1 and throughout the specification". Final Action at page 3. This statement misses the point. Patents "are written to enable those skilled in the art to practice the invention, not the public." *W.L. Gore & Assoc., Inc. v Garlock, Inc.,* 721 F.2d 1540, 1556 (Fed. Cir. 1983). Further, there is a strong presumption that the application as filed contains an adequate written description of the claimed invention. *In re Wertheim*, 541 F.2d 257, 263, (C.C.P.A. 1976). One of ordinary skill in the art reading the specification would recognize that page 34, line 21 to page 35, line 8 and Example 1 at page 88 disclose that SEQ ID NO: 1 can be used as a marker of cold tolerance. The specification need not contain an explicit statement to that effect.

An Examiner must accept a utility by an Applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See*, *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992), emphasis added. "More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." Federal Register 66(4):1096, Utility Guidelines (2001), emphasis added. The Examiner asserts "[i]t would require significant study to identify the actual function of the

maize protein [encoded by SEQ ID NO: 1] ..." Final Action at page 4. However, the Examiner has neither provided sufficient evidence nor sound scientific reasoning to support this assertion.

What the Examiner has provided, at most, are a few general scientific publications indicating that sequence and structural homology apparently cannot rigorously be correlated with functionality. The Examiner cites various articles (Bork *et al.*, *Genome Res.* **10**, 398-400, 2000; Skolnick *et al.*, *Trends Biotech.* **18(1)**, 34-39, 2000; Doerks *et al. Trends Genet.* **14**, 248-250, 1998; Smith *et al.*, *Nature Biotech.* **15**, 1222-1223, 1997; Brenner, *Trends Genet.*, **15**, 132-133, 1999; and Bork, *Trends Genet.*, **12**, 425-427, 1996), Final Action at page 6, that are general references allegedly indicating that protein function cannot be rigorously predicted from structure. This is not enough.

"[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *See, Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565 (Fed. Cir. 1996), emphasis added. Any challenge to an Applicant's assertion of utility must be supported by sound scientific reasoning or sufficient evidence and because the Examiner has provided neither she retains the initial burden of challenging the presumptively correct assertion of utility. *Brana*, 51 F.3d at 1567. The Examiner cannot shift this burden to Appellants.

Appellants respectfully submit that unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See, In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. Pat. App. Int. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement). It is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention."

Johns Hopkins University v. CellPro, 152 F.3d 1342, 1361 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991).

In conclusion, Appellants respectfully submit that the claimed invention has a credible, substantial, specific or well-established utility and respectfully request that the Board reverse the rejection of claims 1 and 8 to 13 under 35 U.S.C. § 101.

C. The Claimed Nucleic Acids Satisfy the Enablement Requirement of 35 U.S.C. § 112

The Examiner rejected claims 1 and 8 to 13 under 35 U.S.C. § 112, first paragraph, because the claimed invention is allegedly "not supported by either a 'specific or substantial' asserted utility or a well-established utility" and therefore "one skilled in the art would not know how to use the claimed invention." Final Action at page 3. Appellants submit that this rejection has been overcome by the arguments set forth above with respect to the rejection under 35 U.S.C. § 101.

Using the *Wands* factors the Examiner takes the position that it would require "undue experimentation to make and/or use the claimed invention in its full scope." Final Action at page 6. Appellants respectfully disagree. Not only is it well established patent jurisprudence that Appellants need not teach "conventional and well-known genetic engineering techniques" (*see, e.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345 (Fed. Cir. 2000)), which would include the use of the claimed sequence with other nucleic acid sequences, but Appellants also submit that an analysis of the criteria presented by *In re Wands* supports Appellants' position that no undue experimentation would be required to make and use the claimed invention. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1998).

The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and radiometric synthase assay conditions, to which a person of ordinary skill in the art has access. Performing routine and well-known steps cannot create undue experimentation even if it is laborious. *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976). The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. The specification provides seven Examples, based on which one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth, fifth and sixth *Wands* criteria focus on the nature of the invention, the state of the art and the relative skill in the art. The present invention relates to nucleic acid sequences, and the specification further describes amino acid sequences derived therefrom, antibodies, constructs and methods related thereto. *See, e.g., Specification* at page 29, line 5 through page 30, line 20 (describing polypeptide molecules and homologues), and page 34, line 3 through page 88, line 3 (describing use of the claimed nucleic acid molecules in methods of transforming plants). Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm and introduce into other hosts, nucleic acid and amino acid sequences.

The seventh *Wands* criterion considers the predictability of the art. The Examiner has presented no evidence why one of ordinary skill in the art would not, for example, be able to predict substitutions or use the nucleic acid molecules of the present invention in the disclosed

uses. Appellants assert that the specification discloses sufficient guidance, for example through the Examples, to render these results predictable.

The subject matter of the pending claims has been disclosed in the specification in a manner adequate to enable one of skill in the art to make and use the claimed invention without undue experimentation. Appellants have disclosed the complete chemical structure of SEQ ID NO: 1. For example, given the complete chemical structure of SEQ ID NO: 1, one of ordinary skill in the art would understand how to use the sequence of SEQ ID NO: 1 for the uses disclosed in the specification, *e.g.*, identifying promoters and associated regulatory sequences (page 36, line 16 through page 38, line 6), and identifying polymorphisms (page 39, line 6, through page 46, line 3). As stated above, Appellants need not teach conventional and well-known genetic engineering techniques. Finally, as previously stated, the performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See*, *In re Wands*, 858 F.2d at 737; *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976).

Appellants respectfully submit that the claimed invention has a credible, substantial, specific or well-established utility and respectfully request that the Board reverse the rejection of claims 1 and 8 to 13 under 35 U.S.C. § 112, first paragraph.

D. The Claimed Nucleic Acids Satisfy the Written Description Requirement of 35 U.S.C. § 112

The Examiner rejected claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Final Action at page 7.

The purpose of the written description requirement is to ensure that the inventor had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479 (Fed. Cir. 1998);

Lockwood v. American Airlines, 107 F.3d 1565, 1572 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996). In accordance with this purpose, Appellants need not "describe," in the sense of 35 U.S.C. § 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251 (Fed. Cir. 1989).

A related, and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston-Purina Co. v. Far-Mar Co*, 772 F.2d 1570, 1575 (Fed. Cir. 1985), *quoting In re Rasmussen*, 650 F.2d 1212, 1215 (C.C.P.A. 1981). Thus, in order for Appellants to describe each and every molecule encompassed by the claims, it is not required that every aspect of those nucleic acid molecules be disclosed. *In re Alton*, 76 F.3d at 1175 (if a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if not every nuance, then the written description requirement has been met). Indeed, recently, the Federal Circuit stated that "[i]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention." *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

The fact that the claims at issue are intended to cover molecules that include the recited sequence joined with additional sequences, or complements of the recited sequence, does not

mean that Appellants were any less in possession of the claimed nucleic acid molecules.[1] It is well-established law that use of the transitional term "comprising" properly leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271 (Fed. Cir. 1986).

The Examiner states that "[c]laim 1 is directed to a maize protein." and "[t]he breadth of enablement is not commensurate in scope with the claims." Final Action at page 7. Appellants respectfully disagree with the Examiner's characterization of claim 1 and submit that claim 1 actually recites "[a] substantially purified nucleic acid molecule that encodes a maize protein comprising a nucleic acid sequence of SEQ ID NO: 1 or its complement." It appears that the Examiner's position is that there is no written description of the nucleic acid sequence of SEQ ID NO: 1 which encodes the maize protein. This is clearly untrue because the specification demonstrates to one skilled in the art that Appellants were in possession of the claimed genera of nucleic acid molecules.

The Examiner states that the specification apparently "discloses very narrow working examples as compared to the wide breath (*sic*) of the claims". Final Action at page 7. The Applicants respectfully remind the Examiner that not only does the present application describe the nucleic acid molecule recited by claim 1 (SEQ ID NO: 1) but it also describes gene sequences, corresponding sequences from other species, mutated sequences, SNPs, polymorphic

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[1] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then it goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751 (C.C.P.A. 1972).

sequences, promoter sequences, exogenous sequences, and so forth (*Specification* at page 10, lines 1 to 7; page 22, line 9 to page 25, line 20; page 26, line 8 to page 27, line 20, and page 36, line 16 to page 38, line 6). The specification also describes appropriate hybridization conditions (*Specification* at page 19, line 1 to page 20, line 12); fusion protein or peptide molecules or fragments thereof encoded by the nucleic acid molecules of the present invention (*Specification* at page 29, line 23 to page 30, line 2); plant homologue proteins (*Specification* at page 30, lines 3 to 19); site directed mutagenesis of the claimed nucleic acid molecules (*Specification* at page 59, line 12 to page 60, line 7); and vectors comprising the claimed nucleic acid molecules and methods of transforming plants (*Specification* at page 64, line 13 to page 72, line 6). Moreover, the specification describes the construction of maize cDNA libraries and sequences obtained from maize cDNA libraries (*Specification* at page 34, line 4 to page 35, line 8 and page 88, line 5 through page 97, line 23).

Appellants have disclosed common structural features, for example the nucleotide sequence of SEQ ID NO: 1. Thus, for example, if a particular nucleic acid molecule contains the nucleotide sequence of SEQ ID NO: 1, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1. Moreover, related nucleic acid molecules falling within the scope of the claimed invention are readily identifiable – they either contain the nucleic acid sequence of SEQ ID NO: 1 or they do not. The fact that the nucleic acid molecules may comprise additional sequences is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the specification.

The Examiner also states that "(t)he [Appellants' previous] response does not have arguments regarding what is the nucleic acid sequence which encodes the fragment thereof

recited in claim 1." Final Action at page 7. Appellants respectfully note that claim 1 does not recite fragments of SEQ ID NO: 1.

In conclusion, Appellants respectfully submit that claim 1 is supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Board reverse the rejection of claim 1 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the foregoing, Appellants respectfully request that the Board of Patent Appeals and Interferences reverse the pending rejections and that the subject application be allowed forthwith.

Respectfully submitted,

Date: May 11, 2007

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CLAIMS APPENDIX

Claim 1. A substantially purified nucleic acid molecule that encodes a maize protein comprising a nucleic acid sequence of SEQ ID NO: 1 or its complement.

Claim 8. A substantially purified nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 or its complement.

Claim 9. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule consists of a nucleic acid sequence of SEQ ID NO: 1 or its complement.

Claim 10. A substantially purified first nucleic acid molecule comprising a fragment from about 50 to about 100 nucleotide residues, wherein said fragment exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and its complement.

Claim 11. The substantially purified first nucleic acid molecule according to claim 10, wherein said first nucleic acid molecule consists of said fragment.

Claim 12. The substantially purified first nucleic acid molecule according to claim 10, wherein said substantially purified nucleic acid molecule further comprises a region having a single nucleotide polymorphism.

Claim 13. A substantially purified nucleic acid molecule comprising a fragment nucleic acid molecule, wherein said fragment consists of about 50 to about 100 nucleotide residues of the nucleic acid molecule of SEQ ID NO: 1 or its complement.

EVIDENCE APPENDIX

None

RELATED PROCEEDINGS APPENDIX

1. *Ex parte Fisher*, 72 U.S.P.Q.2d 1020 (Bd. Pat. App. Int. 2004);
2. *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005);
3. Appeal Brief filed in U.S. Patent Application Serial No. 09/684,016;
4. Appeal Brief filed in U.S. Patent Application Serial No. 10/361,942;
5. Appeal Brief filed in U.S. Patent Application Serial No. 09/199,129;
6. Appeal Brief filed in U.S. Patent Application Serial No. 09/920,953;
7. Appeal Brief filed in U.S. Patent Application Serial No. 09/663,423;
8. Appeal Brief filed in U.S. Patent Application Serial No. 09/237,183; and
9. Appeal Brief filed in U.S. Patent Application Serial No. 10/437,963.

Ex parte Fisher

U.S. Patent and Trademark Office Board of Patent Appeals and Interferences

Appeal No. 2002-2046

Decided April 1, 2004

PATENTS

[1] Patentability/Validity -- Utility (§ 115.10)

Invention must have "substantial" utility in order to be "useful" within meaning of 35 U.S.C. § 101, since, if Section 101's requirement is given its broadest reach, then little or nothing of chemical nature would be found to lack utility; thus, invention must provide specific benefit in its currently available form, and vague, general disclosures or arguments that invention is "useful in research," or statements that invention is capable of being used for particular purpose, would not satisfy Section 101.

[2] Patentability/Validity -- Utility (§ 115.10)

Disclosed use of claimed nucleic acid molecules encoding maize protein in identifying and detecting polymorphisms in population of maize plants does not provide "substantial" degree of utility required for invention to be "useful" within meaning of 35 U.S.C. § 101, since specification does not explain why claimed nucleotide molecules would in fact be useful in detecting polymorphisms, and since, without further information regarding gene represented by molecules, detection of presence or absence of polymorphism provides only barest information concerning genetic heritage.

[3] Patentability/Validity -- Utility (§ 115.10)

Disclosed use of claimed nucleic acid molecules encoding maize protein to isolate nucleic acid molecules of other plants and organisms does not provide "substantial" degree of utility required for invention to be "useful" within meaning of 35 U.S.C. § 101, since specification does not attribute any property, in terms of plant trait or phenotype, to any of disclosed nucleotide molecules, and absent such information, using claimed molecules to isolate other molecules does not represent substantial utility; applicants' assertion that claimed nucleic acid molecules may be useful in searching for certain promoters does not supply required utility, since specification does not provide any expectation of successfully using any of claimed molecules to isolate such promoters, and since there is no evidence that claimed molecules are tissue or cell-type specific, or developmentally or environmentally regulated.

[4] Patentability/Validity -- Utility (§ 115.10)

Invention can have utility shared by other compounds or compositions, but not every utility will satisfy requirements of 35 U.S.C. § 101, even if utility is shared by class of inventions; thus, although utility need not be unique to claimed invention, it must nevertheless be specific, and in currently available form, in order to satisfy Section 101.

[5] Patentability/Validity -- Utility (§ 115.10)

Assertion that claimed nucleic acid molecules encoding maize protein can be introduced into plant or plant cell, which can then be used to screen for compounds such as herbicides, does not provide "substantial" degree of utility required for invention to be "useful" within meaning of 35 U.S.C. § 101, since invention claims otherwise uncharacterized nucleic acid molecule, not "cell-based assay," and since specification does not indicate that asserted screening method is feasible if uncharacterized nucleic acid is used.

[6] Patentability/Validity -- Utility (§ 115.10)

Disclosed use of claimed nucleic acid molecules encoding maize protein as components of assays for monitoring gene expression does not provide "substantial" degree of utility required for invention to be "useful" within meaning of 35 U.S.C. § 101, since specification provides no guidance that would allow person skilled in art to use data relating to expression of gene in any practical way; claim that those skilled in art could experiment with claimed nucleic acids and figure out for themselves what results might mean does not provide "specific benefit in currently available form," and although each nucleic acid used in gene expression assay contributes to data generated by assay as whole, fact that assay itself may have patentable utility does not mean that each tiny component of assay also has patentable utility.

[7] Patentability/Validity -- Specification -- Written description (§ 115.1103)

Application claiming five nucleic acid molecules encoding maize protein was improperly rejected for failure to satisfy written description requirement of 35 U.S.C. § 112, since application provides nucleotide sequences for five molecules, and claim's use of "comprising" allows for addition of nucleotides or other molecules at either end of nucleotide sequences without permitting internal alterations of sequences, and since fact that claimed molecules may have other molecules attached at their ends does not diminish adequate written description of molecules having sequences set forth in application.

***1021** Patent application of Dane K. Fisher and Raghunath V. Lalgudi, serial no. 09/619,643 (nucleic

acid molecule encoding maize protein or fragment thereof). Applicants appeal from examiner's final rejection of sole claim pending in application. Affirmed in part and reversed in part.

[Editor's Note: The Board of Patent Appeals and Interferences states that this opinion was not written for publication, and is not binding precedent of the board.]

Lawrence M. Lavin Jr., Monsanto Co., St. Louis, Mo., for applicants.

Before William F. Smith, Adams, and Grimes, administrative patent judges.

Adams, J.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, the only claim pending in the application, reproduced below:

1.A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5.

The examiner does not rely on a reference.

GROUNDS OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claim 1 also stands rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility and enablement rejections. We reverse the written description rejection.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags (ESTs). *See* Specification, page 15, lines 9-10. ESTs "are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9, lines 2-4, of appellants' specification "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of ***1022** SEQ ID NO: 1 through SEQ ID NO: 32236." Of these 32,236 nucleic acid sequences, the originally filed claims where directed to SEQ ID NO: 1 through SEQ ID NO: 4,013. On January 26, 2001 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, *inter alia*, appellants "to elect up to 5 nucleic acid sequences" for consideration on the merits. Paper No. 4, page 3. In response, appellants elected SEQ ID NO:1 through SEQ ID NO:5. The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO: 5 are disclosed to be obtained from cDNA library LIB3115 "generated from maize (RX601, Asgrow Seed Company, Des Moines, Iowa U.S.A.) pooled leaf tissue. . .." Specification, pages 79-80, Example 1.

The specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 which are summarized by the examiner (Answer, bridging paragraph, pages 5-6) as follows:

The specification teaches that the nucleic acids may be used to produce a plant containing reduced levels of a protein (pg. 11), determining an association between a polymorphism and a plant trait (pg. 11), isolating a genetic region or nucleic acid (pg. 11), determining a level or pattern in a plant cell of a protein in a plant (pg. 11), determining a mutation in a plant whose presence is predictive of a mutation affecting a level or pattern of a protein (pg. 13), as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function (pg. 14), and identifying tissues (pg. 14)[.] The specification states that the nucleic acid ESTs of the present invention can enable the acquisition of molecular markers, which can be used in breeding schemes, genetic and molecular mapping and cloning of agronomically significant genes (pg. 31).

In the examiner's opinion "[t]hese are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed." Answer, page 6. For example, the examiner finds (Answer, page 10), "determining whether the claimed nucleic acids have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way." [FN1]

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. *See e.g.*, Brief, pages 6- 12. According to appellants

(Brief, page 3), "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of maize plants." Furthermore, appellants assert (Brief, page 8), "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms. . .."

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5. According to appellants' specification (page 15, lines 19-25), the term "substantially purified"

refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the claimed invention the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ***1023** ID NO: 1 through SEQ ID NO: 5. [FN2] In this regard, we recognize, as does the examiner (Answer, page 14), the claim as written encompasses, *inter alia*, genes, full open reading frames, fusion constructs, and cDNAs.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, selected from the group consisting of the nucleic acid molecule defined by the 429 nucleotide sequence set forth in SEQ ID NO: 1, the 413 nucleotide sequence set forth in SEQ ID NO: 2, the 365 nucleotide sequence set forth in SEQ ID NO: 3, the 414 nucleotide sequence set forth in SEQ ID NO: 4, and the 333 nucleotide sequence set forth in SEQ ID NO: 5, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5 possesses utility under 35 U.S.C. § 101 is *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in *Brenner*, at 534-35, 148 USPQ at 695 [FN3] ,

the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the *Brenner* court's statement that a patent should issue only when an invention possesses "substantial utility," *i.e.*, "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. *Cross v. Iizuka*, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in *Brenner* was a claim to "a chemical process which yields an already known product whose utility--other than as a possible object of scientific inquiry--ha[d] not yet been evidenced." *Id.* at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. *See id.* at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." *Id.* at 522, 148 USPQ at 691.

The *Brenner* Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." *Id.* at 529, 148 USPQ at 693. Thus,

[i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful"

phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"--if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694. [FN4]

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." *Id.* at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until ***1024** a process is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." *Id.* at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." *Id.* at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." *Id.* at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." *Id.*

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101' s utility requirement. The first opinion of the CCPA applying *Brenner* was *In re Kirk*, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in *Kirk* was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." *Id.* at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." *Id.* at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. *Id.* at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are--or are not--in fact useful or possess useful properties, and to ascertain what those properties are." *Id.* at 942, 153 USPQ at 53.

The *Kirk* court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by *Brenner*. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in *Brenner*. *See Kirk*, 376 F.2d at 945, 153 USPQ at 55.

More recently, in *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in *Ziegler* claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene

or its film that demonstrated its utility." *Id.* The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. *Id.* "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." *Id.*

On the other hand, the CCPA reversed a rejection for lack of utility in *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in *Jolles* claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. ***1025***See id.* at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." *Id.*, 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. *See id.* at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," *id.* at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. *See id.* at 1327-28, 206 USPQ at 891.

The Federal Circuit held in *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that *in vivo* testing (as in *Jolles*) was not necessarily required to show utility in the pharmaceutical context. The *Cross* court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." *Id.* at 1044, 224 USPQ at 742 (citing *Brenner v. Manson*). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question." *Id.* at 1051, 224 USPQ at 748. Successful *in vitro* testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds . . . , analogous to the benefit provided by the showing of an *in vivo* utility." *Id.* On the facts of that case -- successful *in vitro* testing supplemented by similar *in vitro* and *in vivo* activities of structurally similar compounds -- the court held that *in vitro* activity was sufficient to meet the requirements of § 101. *See id.*

The Federal Circuit confirmed in *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in *Brana* was a group of compounds disclosed to have antitumor activity. *See id.* at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of *in vivo* activity against tumors in a mouse model. *See id.*, 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. *See id.* at 1567, 34 USPQ2d at 1442.

> [1] Several lessons can be drawn from *Brenner* and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. *See Brenner*, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in *Brenner* was useful as a possible object of scientific inquiry, and the polypropylene claimed in *Ziegler* was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. *See Brenner*, 383 U.S. at 529, 148 USPQ at 696; *Ziegler*, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a *de minimis* standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. *Brenner*, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (*Jolles*, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful *in vitro* testing supplemented by similar *in vitro* and *in vivo* activities of structurally similar compounds (*Cross*, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing *in vivo* antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (*Brana*, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, *Brenner's* standard has been interpreted to mean that "vague, general disclosures or

arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. *See Kirk*, 376 F.2d at 945, 153 USPQ at 55 (interpreting *Brenner*). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. *Ziegler*, at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted ***1026** in the specification, two have received the most attention in the briefing in this appeal, *i.e.*, identification and detection of polymorphisms and use as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. *Polymorphisms*

[2] This utility is discussed at pages 35-42 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5. To the contrary, according to appellants' specification (page 35, lines 25-26), "one or more of the [32,236] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify . . . polymorphism(s)." The specification does not explain why any of the 32,236 nucleotide molecules disclosed in the specification, or more specifically the five nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a *substantial* utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, bridging paragraph, pages 10-11):

Polymorphisms are natural variations within sequences which themselves may not have any meaningful use. Therefore, determining whether the claimed nucleic acids [(or nucleic acids detected by the claimed nucleic acids)] have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way. The [a]ppellant also argues, "many of these uses are directly analogous to a microscope". This argument has been reviewed but is not convincing because the microscope provides information to the scientist which is automatically useful. For example, the microscope may be used for identification and differentiation between gram-positive and gram-negative bacteria. The differentiation of bacteria facilitates in the administration of proper antibiotics. For example, if the microscope is used to determine whether Staph is present or whether Strep is present provides valuable information to the scientist and/or doctor for treating patients. The instant invention, however, provides no information to this extent. If the scientist determines that SEQ ID NO: 1 is present, the scientist does not know how to use this information. Thus, the identification of SEQ ID NO: 1 is not a substantial utility.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. *Probes or source of primers*

[3] Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms. . .." Appeal Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to any of the nucleotide molecules set

> forth in SEQ ID NO: 1 through SEQ ID NO: 5. In the absence of such information, using the claimed molecules to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a ***1027** "chromosome walk." Brief, pages 8-9. According to appellants (Brief, page 9),

> The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in leaves at the time of anthesis. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at that important developmental state, including proteins that provide disease resistance. Because the claimed nucleic acid molecules were isolated from leaves, they provide an appropriate starting point for isolating a promoter active in leaves. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

As we understand this argument, the claimed ESTs may be useful in searching for promoters that are only active in leaves at the time of anthesis. The specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5 would be useful in obtaining a successful result from such a search. As set forth at page 34, lines 14-19 of appellants' specification,

> The [32,236] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 32,236 nucleic acid molecules disclosed in the specification, or more specifically the five nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell-type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding appellants' assertion (Brief, page 9), there is no evidence on this record that any of the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are tissue or cell-type specific, or developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA library LIB3115. Specification, page 80, lines 5-6. There is no evidence on this record that LIB3115 is a subtractive cDNA library, wherein nucleic acid molecules from other maize tissue, or from other developmental stages, was subtracted (removed) from the library. Compare, for example, the subtractive cDNA library LIB3153 which is disclosed (specification, page 83, lines 17-19) to be "generated by subtracting driver cDNA, which is prepared from kernels harvested from 15 DAP [days after pollination] maize plants, from target cDNA, which is prepared from endosperms harvested from 5-8 day[s] after pollination (DAP) maize plants." In contrast to the claimed nucleic acid molecules, nucleic acid molecules SEQ ID NO: 24,931 through SEQ ID NO: 25,680 are from the subtractive cDNA library LIB3153.

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NO: 1 through SEQ ID NO: 5, represent five randomly selected nucleic acid molecules isolated from pooled leaf tissue at the time of anthesis. Notwithstanding appellants' emphasis on "anthesis," for the foregoing reasons, we find no evidence on this record that any of appellants' five randomly selected nucleic acid molecules are expressed only at the time of "anthesis." Accordingly, despite appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in leaves at the time of anthesis. As appellants recognize (Brief, page 9), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

We recognize appellants' argument (Brief, bridging sentence, pages 9-10), "[a]n invention may be 'less effective than existing devices but nevertheless meet the statutory criteria for patentability.' *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility

sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit ***1028** in currently available form. *See, e.g., Brenner*, 383 U.S. at 534, 148 USPQ at 695.

[4] An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. *Other Arguments*

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief, page 6. Specifically, appellants argue (*id.*) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay"which appellants assert to have a "legally sufficient utility." *Id.*

[5] Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 73, line 17 through page 74, line 17) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized [FN5] as here. Such a use does not provide a specific or substantial benefit in currently available form.

[6] Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology and use as molecular markers. Brief, page 6. In regard to microarrays, appellants argue (*id.* fn. 3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that the asserted utility of the claimed nucleic acid--as one component of an assay for monitoring gene expression--does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in e.g., SEQ ID NO: 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean. As the examiner points out (Answer, page 9), "the instant claimed nucleic acids appear to require further experimentation on the material itself to determine the function and properties of the claimed nucleic acids."

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint as to what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

***1029** In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to *Brenner*. In *Brenner*, the applicant

claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. *Id.* at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in *Brenner* lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Assuming *arguendo*, that a generic gene expression assay--one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid--its data point--is only a tiny contribution to the overall picture. The *Brenner* Court held that § 101 sets more than a *de minimis* standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. *See Brenner*, 383 U.S. at 534, 148 USPQ at 695. The *Brenner* Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility -- a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. *See id.*

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 in such devices represents a substantial use.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, page 13, emphasis removed), "since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth [in support of the rejection under 35 U.S.C. § 101] one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

***1030** Written description

This rejection stands on a different footing. As we understand the examiner's argument the use of the transitional phrase "comprising" in appellants' claimed invention results in appellants claiming a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO: 1 through SEQ ID NO: 5. Answer, pages 13-16. Apparently the examiner is of the opinion that the claimed invention should be limited to nucleic acid molecules as set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In response appellants argue (Brief, page 14, original footnote omitted),

Applicants have provided the nucleotide sequences required by the claims, *i.e.*, SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences [[FN6]] does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules.

[7] As discussed *supra*, as we understand the claimed invention, the use of the transitional term "comprising"does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. We agree with appellants that they have provided an adequate written description of nucleic acid molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. That the claimed nucleic acid molecules may have other molecules attached to either, or both of their 5' or 3' ends does not diminish appellants' adequate written description of the nucleic acids molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5 as claimed.

Accordingly, we reverse the rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

FN1. During the Oral Hearing, appellants' representative confirmed that the administrative file contained no evidence that the claimed ESTs where capable of detecting a polymorphism that correlated with any particular trait.

FN2. This interpretation of the claimed invention was confirmed by appellants' representative during the Oral Hearing.

FN3. In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since *Brenner*, have used the phrases "substantial utility" and "practical utility" interchangeably. *See e.g.*, *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1963-1964,39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

FN4. The invention at issue in *Brenner* was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." *Id.* at 535, 148 USPQ at 695-96.

FN5. To emphasize the uncharacterized nature of appellants' invention we note the examiner's finding (Answer, page 17) that translating SEQ ID NO: 5 in all 6 possible reading frames reveals that the sequence contains numerous stop codons which would terminate the translation of a protein, or protein fragment, encoded thereby.

FN6. By way of examples appellants explain (Brief, bridging paragraph, pages 14-15) that the specification discloses, *inter alia*, the claimed nucleic acid molecules joined together with vectors, and other nucleic acids (e.g. fusion nucleic acid molecules) and detectable labels.

982 F.2d 1554, 1560 (Fed.Cir.1992) (holding a C.F.R. provision invalid because it did not "comport with the clear statutory mandate"). Because § 831.2203(f) conflicts with and is no longer supported by the amendments to § 8343a, it is ineffective. Resort to that regulation to affect an AFA following the effective dates of amendments is foreclosed.

Here, Kievenaar's husband completed the annuity paperwork in February 2002. His annuity was to begin on July 1, 2002, and he died suddenly on July 22, 2002. Thus, his annuity commenced at a time when § 831.2203(f) was ineffective. While we are sympathetic to Kievenaar's position, we have no alternative but to conclude that she is not eligible for the AFA she seeks.

Because the unavailability of § 831.2203(f) during the period relevant to Kievenaar is dispositive of her case, we need not and do not decide the issue of validity of the regulation prior to the effective dates of the amendments to § 8343a.

CONCLUSION

The Board correctly determined that 5 C.F.R. § 831.2203(f) was inapplicable to Kievenaar's request to change her husband's self-only annuity to an AFA. The Board's affirmance of OPM's decision to deny the requested AFA was in accordance with law and is affirmed.

AFFIRMED

In re Dane K. FISHER and Raghunath V. Lalgudi.

No. 04–1465.

United States Court of Appeals, Federal Circuit.

Sept. 7, 2005.

Background: Applicants for patent covering "expressed sequence tags" for identifying nucleic acid sequences in maize genes challenged decision of United States Patent and Trademark Office Board of Patent Appeals and Interferences, 72 U.S.P.Q.2d 1020, 2004 WL 2185929, finding their claim unpatentable for lack of utility and lack of enablement.

Holdings: The Court of Appeals, Michel, Chief Judge, held that:

(1) claimed invention lacked specific and substantial utility, and

(2) application failed for lack of enablement.

Affirmed.

Rader, Circuit Judge, dissented and filed opinion.

1. Patents ⇨314(5)

Whether patent application discloses requisite utility for claimed invention is question of fact. 35 U.S.C.A. § 101.

2. Patents ⇨48

Patent application covering "expressed sequence tags" for identifying nucleic acid sequences in maize genes lacked requisite utility where tagged genes had no known functions; claimed tags acted as no more than research intermediates that might help scientists to isolate particular underlying protein-encoding genes and conduct further experimentation on those genes. 35 U.S.C.A. § 101.

3. Patents ⚿46

To be patentable, claimed invention must have substantial and specific "utility," i.e., invention must have significant and presently available benefit to public, and its claimed use must not be so vague as to be meaningless. 35 U.S.C.A. § 101.

See publication Words and Phrases for other judicial constructions and definitions.

4. Evidence ⚿48

Patents ⚿97

Manual of Patent Examining Procedure (MPEP) and Patent and Trademark Office's Utility Guidelines are not binding on court ruling on patent's validity, but may be given judicial notice to extent they do not conflict with patent statutes.

5. Patents ⚿99

Patent application for invention that lacks requisite utility also fails, as matter of law, for lack of enablement. 35 U.S.C.A. §§ 101, 112(1).

Seth P. Waxman, Wilmer Cutler Pickering Hale and Dorr LLP, of Washington, DC, argued for appellants. With him on the brief were William F. Lee and Richard W. O'Neill, of Boston, Massachusetts; and William G. McElwain and Henry N. Wixon, of Washington, DC.

Stephen Walsh, Associate Solicitor, United States Patent and Trademark Office, of Arlington, Virginia, argued for the Director of the Patent and Trademark Office. With him on the brief were John M. Whealan, Solicitor, and Thomas W. Krause, Associate Solicitor.

Joseph A. Keyes, Jr., of Washington, DC, for amicus curiae Association of American Medical Colleges.

Marc S. Gold, of Washington, DC, for amicus curiae National Academy of Sciences.

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Darrel C. Karl, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., of Washington, DC, for amicus curiae American College of Medical Genetics.

Jeffrey P. Kushan, Sidley Austin Brown & Wood, LLP, of Washington, DC, for amicus curiae Genentech, Inc. With him on the brief were Kathi A. Cover and David L. Fitzgerald.

George C. Yu, of Emeryville, California, for amicus curiae Affymetrix, Inc.

Before MICHEL, Chief Judge, RADER and BRYSON, Circuit Judges.

Opinion for the court filed by Chief Judge MICHEL.

Dissenting opinion filed by Circuit Judge RADER.

MICHEL, Chief Judge.

Dane K. Fisher and Raghunath Lalgudi (collectively "Fisher") [1] appeal from the decision of the U.S. Patent and Trademark Office ("PTO") Board of Patent Appeals and Interferences ("Board") affirming the examiner's final rejection of the only pending claim of application Serial No. 09/619,-

1. The real party in interest is Monsanto Technology LLC, which is owned by the Monsanto Company.

643 (the "'643 application"), entitled "Nucleic Acid Molecules and Other Molecules Associated with Plants," as unpatentable for lack of utility under 35 U.S.C. § 101 and lack of enablement under 35 U.S.C. § 112, first paragraph. *Ex parte Fisher*, App. No.2002–2046 (Bd.Pat.App.Int. Mar. 16, 2004) ("*Board Decision*"). This appeal was submitted after oral argument on May 3, 2005. Because we conclude that substantial evidence supports the Board's findings that the claimed invention lacks a specific and substantial utility and that the '643 application does not enable one of ordinary skill in the art to use the invention, we affirm.

I. BACKGROUND

A. Molecular Genetics and ESTs

The claimed invention relates to five purified nucleic acid sequences that encode proteins and protein fragments in maize plants. The claimed sequences are commonly referred to as "expressed sequence tags" or "ESTs." Before delving into the specifics of this case, it is important to understand more about the basic principles of molecular genetics and the role of ESTs.

Genes are located on chromosomes in the nucleus of a cell and are made of deoxyribonucleic acid ("DNA"). DNA is composed of two strands of nucleotides in double helix formation. The nucleotides contain one of four bases, adenine ("A"), guanine ("G"), cytosine ("C"), and thymine ("T"), that are linked by hydrogen bonds to form complementary base pairs (*i.e.*, A–T and G–C).

When a gene is expressed in a cell, the relevant double-stranded DNA sequence is transcribed into a single strand of messenger ribonucleic acid ("mRNA"). Messenger RNA contains three of the same bases as DNA (A, G, and C), but contains uracil ("U") instead of thymine. mRNA is released from the nucleus of a cell and used by ribosomes found in the cytoplasm to produce proteins.

Complementary DNA ("cDNA") is produced synthetically by reverse transcribing mRNA. cDNA, like naturally occurring DNA, is composed of nucleotides containing the four nitrogenous bases, A, T, G, and C. Scientists routinely compile cDNA into libraries to study the kinds of genes expressed in a certain tissue at a particular point in time. One of the goals of this research is to learn what genes and downstream proteins are expressed in a cell so as to regulate gene expression and control protein synthesis.[2]

An EST is a short nucleotide sequence that represents a fragment of a cDNA clone. It is typically generated by isolating a cDNA clone and sequencing a small number of nucleotides located at the end of one of the two cDNA strands. When an EST is introduced into a sample containing a mixture of DNA, the EST may hybridize with a portion of DNA. Such binding shows that the gene corresponding to the EST was being expressed at the time of mRNA extraction.

Claim 1 of the '643 application recites:

> A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5.

The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO: 5 are obtained from cDNA library LIB3115, which was generated from pooled leaf tissue harvested

2. We have discussed the basic principles of molecular genetics more extensively in prior cases. *See, e.g., In re Deuel*, 51 F.3d 1552, 1554–56 (Fed.Cir.1995); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1207–08 (Fed.Cir.1991); *In re O'Farrell*, 853 F.2d 894, 895–99 (Fed.Cir.1988).

from maize plants (RX601, Asgrow Seed Company, Des Moines, Iowa, U.S.A.) grown in the fields at Asgrow research stations. SEQ ID NO:1 through SEQ ID NO:5 consist of 429, 423, 365, 411, and 331 nucleotides, respectively. When Fisher filed the '643 application, he claimed ESTs corresponding to genes expressed from the maize pooled leaf tissue at the time of anthesis. Nevertheless, Fisher did not know the precise structure or function of either the genes or the proteins encoded for by those genes.

The '643 application generally discloses that the five claimed ESTs may be used in a variety of ways, including: (1) serving as a molecular marker for mapping the entire maize genome, which consists of ten chromosomes that collectively encompass roughly 50,000 genes; (2) measuring the level of mRNA in a tissue sample via microarray technology to provide information about gene expression; (3) providing a source for primers for use in the polymerase chain reaction ("PCR") process to enable rapid and inexpensive duplication of specific genes; (4) identifying the presence or absence of a polymorphism; (5) isolating promoters via chromosome walking; (6) controlling protein expression; and (7) locating genetic molecules of other plants and organisms.

B. Final Rejection

In a final rejection, dated September 6, 2001, the examiner rejected claim 1 for lack of utility under § 101. The examiner found that the claimed ESTs were not supported by a specific and substantial utility. She concluded that the disclosed uses were not specific to the claimed ESTs, but instead were generally applicable to any EST. For example, the examiner noted that any EST may serve as a molecular tag to isolate genetic regions. She also concluded that the claimed ESTs lacked a substantial utility because there was no known use for the proteins produced as final products resulting from processes involving the claimed ESTs. The examiner stated: "Utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities."

The examiner also rejected the claimed application for lack of enablement under § 112, first paragraph. She reasoned that one skilled in the art would not know how to use the claimed ESTs because the '643 application did not disclose a specific and substantial utility for them.

On July 19, 2000, Fisher filed a notice of appeal with the Board.

C. Board Proceedings

The Board considered each of Fisher's seven potential uses but noted that Fisher focused its appeal on only two: (1) use for the identification of polymorphisms; and (2) use as probes or as a source for primers. As to the first, the Board found that the application failed to explain why the claimed ESTs would be useful in detecting polymorphisms in maize plants. *Board Decision*, slip op. at 14. The Board reasoned that "[w]ithout knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage." *Id.*, slip op. at 15. Thus, the Board concluded that Fisher's asserted uses for the claimed ESTs tended to the "insubstantial use" end of the spectrum between a substantial and an insubstantial utility. *Id.*

The Board also concluded that using the claimed ESTs to isolate nucleic acid molecules of other plants and organisms, which themselves had no known utility, is not a substantial utility. *Id.*, slip op. at 16. Specifically, the Board noted that Fisher argued that the "claimed ESTs may be

useful in searching for promoters that are only active in leaves at the time of anthesis." *Id.* The Board found, however, that the application failed to show that the claimed ESTs would be expressed only during anthesis or that they would be capable of isolating a promoter active in maize leaves at the time of anthesis. *Id.*, slip op. at 18.

Additionally, the Board addressed the remaining asserted utilities, highlighting in particular the use of the claimed ESTs to monitor gene expression by measuring the level of mRNA through microarray technology and to serve as molecular markers. The Board found that using the claimed ESTs in screens does not provide a specific benefit because the application fails to provide any teaching regarding how to use the data relating to gene expression. *Id.*, slip op. at 21. The Board analogized the facts to those in *Brenner v. Manson*, 383 U.S. 519, 86 S.Ct. 1033, 16 L.Ed.2d 69 (1966), in which an applicant claimed a process of making a compound having no known use. In that case, the Supreme Court affirmed the rejection of the application on § 101 grounds. Here, the Board reasoned: "Just as the process in *Brenner* lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1–5 specific gene expression data." *Id.*, slip op. at 22. The Board offered a similar rationale for the use of the claimed ESTs as molecular markers. *Id.*, slip op. at 24. Accordingly, the Board affirmed the examiner's rejection of the '643 application for lack of utility under § 101. The Board also affirmed the examiner's rejection of the '643 application for lack of enablement under § 112, first paragraph, since the enablement rejection was made as a corollary to the utility rejection.

Fisher timely appealed. We have jurisdiction over this appeal pursuant to 28 U.S.C. § 1295(a)(4) and 35 U.S.C. §§ 141 and 144.

II. DISCUSSION

[1] Whether an application discloses a utility for a claimed invention is a question of fact. *In re Ziegler*, 992 F.2d 1197, 1200 (Fed.Cir.1993). We consequently review the Board's determination that the '643 application failed to satisfy the utility requirement of § 101 for substantial evidence. *In re Gartside*, 203 F.3d 1305, 1315 (Fed.Cir.2000) ("Because our review of the Board's decision is confined to the factual record compiled by the Board, we accordingly conclude that the 'substantial evidence' standard is appropriate for our review of Board factfindings.").

A. Utility

1.

[2] Fisher asserts that the Board unilaterally applied a heightened standard for utility in the case of ESTs, conditioning patentability upon "some undefined 'spectrum' of knowledge concerning the corresponding gene function." Fisher contends that the standard is not so high and that Congress intended the language of § 101 to be given broad construction. In particular, Fisher contends that § 101 requires only that the claimed invention "not be frivolous, or injurious to the well-being, good policy, or good morals of society," essentially adopting Justice Story's view of a useful invention from *Lowell v. Lewis*, 15 F.Cas. 1018, 1019 (No. 8568) (C.C.D.Mass. 1817). Under the correct application of the law, Fisher argues, the record shows that the claimed ESTs provide seven specific and substantial uses, regardless whether the functions of the genes corresponding to the claimed ESTs are known. Fisher claims that the Board's attempt to

equate the claimed ESTs with the chemical compositions in *Brenner* was misplaced and that several decisions in the field of pharmaceuticals, namely, *Cross v. Iizuka*, 753 F.2d 1040 (Fed.Cir.1985), *Nelson v. Bowler*, 626 F.2d 853 (C.C.P.A.1980), and *In re Jolles*, 628 F.2d 1322 (C.C.P.A.1980), are analogous and support finding utility of the claimed ESTs. Fisher likewise argues that the general commercial success of ESTs in the marketplace confirms the utility of the claimed ESTs. Hence, Fisher avers that the Board's decision was not supported by substantial evidence and should be reversed.

The government agrees with Fisher that the utility threshold is not high, but disagrees with Fisher's allegation that the Board applied a heightened utility standard. The government contends that a patent applicant need disclose only a single specific and substantial utility pursuant to *Brenner*, the very standard articulated in the PTO's "Utility Examination Guidelines" ("Utility Guidelines") and followed here when examining the '643 application. It argues that Fisher failed to meet that standard because Fisher's alleged uses are so general as to be meaningless. What is more, the government asserts that the same generic uses could apply not only to the five claimed ESTs but also to any EST derived from any organism. It thus argues that the seven utilities alleged by Fisher are merely starting points for further research, not the end point of any research effort. It further disputes the importance of the commercial success of ESTs in the marketplace, pointing out that Fisher's evidence involved only databases, clone sets, and microarrays, not the five claimed ESTs. Therefore, the government contends that we should affirm the Board's decision.

Several academic institutions and biotechnology and pharmaceutical companies [3] write as amici curiae in support of the government. Like the government, they assert that Fisher's claimed uses are nothing more than a "laundry list" of research plans, each general and speculative, none providing a specific and substantial benefit in currently available form. The amici also advocate that the claimed ESTs are the objects of further research aimed at identifying what genes of unknown function are expressed during anthesis and what proteins of unknown function are encoded for by those genes. Until the corresponding genes and proteins have a known function, the amici argue, the claimed ESTs lack utility under § 101 and are not patentable.

[3] We agree with both the government and the amici that none of Fisher's seven asserted uses meets the utility requirement of § 101. Section 101 provides: "Whoever invents ... any new and *useful* ... composition of matter ... may obtain a patent therefor ...." (Emphasis added). In *Brenner*, the Supreme Court explained what is required to establish the usefulness of a new invention, noting at the outset that "a simple, everyday word ["useful," as found in § 101] can be pregnant with ambiguity when applied to the facts of life." 383 U.S. at 529, 86 S.Ct. 1033. Contrary to Fisher's argument that § 101 only requires an invention that is not "frivolous, injurious to the well-being, good policy, or good morals of society," the Supreme Court appeared to reject Justice Story's de minimis view of utility. *Id.* at 532–33, 86 S.Ct. 1033 (citation omitted).

3. Amici in support of the government include Affymetrix, Inc., American College of Medical Genetics, Association of American Medical Colleges, Baxter Healthcare Corporation, Dow AgroSciences LLC, Eli Lilly and Company, Genentech, Inc., National Academy of Sciences, and the University of North Carolina School of Law.

The Supreme Court observed that Justice Story's definition "sheds little light on our subject," on the one hand framing the relevant inquiry as "whether the invention in question is 'frivolous and insignificant' " if narrowly read, while on the other hand "allowing the patenting of any invention not positively harmful to society" if more broadly read. *Id.* at 533, 86 S.Ct. 1033. In its place, the Supreme Court announced a more rigorous test, stating:

> The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with *substantial utility.* Unless and until a process is refined and developed to this point—where *specific benefit exists in currently available form*—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

Brenner, 383 U.S. at 534–35, 86 S.Ct. 1033 (emphases added). Following *Brenner*, our predecessor court, the Court of Customs and Patent Appeals, and this court have required a claimed invention to have a specific and substantial utility to satisfy § 101. *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563 (Fed.Cir.1996) ("Consequently, it is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

The Supreme Court has not defined what the terms "specific" and "substantial" mean per se. Nevertheless, together with the Court of Customs and Patent Appeals, we have offered guidance as to the uses which would meet the utility standard of § 101. From this, we can discern the kind of disclosure an application must contain to establish a specific and substantial utility for the claimed invention.

Courts have used the labels "practical utility" and "real world" utility interchangeably in determining whether an invention offers a "substantial" utility. Indeed, the Court of Customs and Patent Appeals stated that " '[p]ractical utility' is a shorthand way of attributing 'real-world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some *immediate benefit to the public.*" *Nelson*, 626 F.2d at 856 (emphasis added).[4] It thus is clear that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the "substantial" utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.

Turning to the "specific" utility requirement, an application must disclose a use which is not so vague as to be meaningless. Indeed, one of our predecessor courts has observed "that the nebulous expressions 'biological activity' or 'biological properties' appearing in the specification convey no more explicit indication of the usefulness of the compounds and how to use them than did the equally obscure expression 'useful for technical and pharmaceutical purposes' unsuccessfully relied upon by the appellant in *In re Diedrich* [318 F.2d 946, 50 C.C.P.A. 1355 (1963)]." *In re Kirk*, 54 C.C.P.A. 1119, 376 F.2d 936, 941 (1967). Thus, in addition to providing a "substantial" utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public.

4. In *Cross*, this court considered the phrase "practical utility" to be synonymous with the phrase "substantial utility." 753 F.2d at 1047, n. 13.

[4] In 2001, partially in response to questions about the patentability of ESTs, the PTO issued Utility Guidelines governing its internal practice for determining whether a claimed invention satisfies § 101. *See* Utility Examination Guidelines, 66 Fed.Reg. 1092 (Jan. 5, 2001). The PTO incorporated these guidelines into the Manual of Patent Examining Procedure ("MPEP"). *See* U.S. Pat. & Trademark Off., Manual of Patent Examining Procedure § 2107 (8th ed.2001, rev. May 2004). The MPEP and Guidelines "are not binding on this court, but may be given judicial notice to the extent they do not conflict with the statute." *Enzo Biochem v. Gen–Probe*, 323 F.3d 956, 964 (Fed.Cir. 2002) (citing *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1180 n. 10 (Fed.Cir.1995)). According to the Utility Guidelines, a specific utility is particular to the subject matter claimed and would not be applicable to a broad class of invention. Manual of Patent Examining Procedure § 2107.01. The Utility Guidelines also explain that a substantial utility defines a "real world" use. In particular, "[u]tilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities." *Id.* Further, the Utility Guidelines discuss "research tools," a term often given to inventions used to conduct research. The PTO particularly cautions that

> [a]n assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. [The PTO] must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm.

Id. The PTO's standards for assessing whether a claimed invention has a specific and substantial utility comport with this court's interpretation of the utility requirement of § 101.

Turning to the parties' arguments, Fisher first raises a legal issue, charging that the Board applied a heightened standard for utility in the case of ESTs. Fisher apparently bases this argument on statements made by the Board in connection with its discussion of whether the claimed ESTs can be used to identify a polymorphism. In that context, the Board stated:

> Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development lies the line between 'utility' and 'substantial utility.' We need not draw the line or further define it in this case because the facts in this case represent the lowest end of the *spectrum*, *i.e.*, an insubstantial use.

Board Decision, slip op. at 15 (emphasis added). Fisher reads the word "spectrum" out of context, claiming that the word somehow implies the application of a higher standard for utility than required by § 101. We conclude, however, that the Board did not apply an incorrect legal standard. In its decision, the Board made reference to a "spectrum" to differentiate between a substantial utility, which satisfies the utility requirement of § 101, and an insubstantial utility, which fails to satisfy § 101. The Board plainly did not announce or apply a new test for assessing the utility of ESTs. It simply followed the Utility Guidelines and MPEP, which mandate the specific and substantial utility test set forth in *Brenner*. Indeed, we note that Example 9 of the PTO's "Revised Interim Utility Guidelines Training Materials" is applicable to the facts here. *See* U.S. Pat. & Trademark Off., Revised Interim Utility Guidelines Training Materials 50–53 (1999), *available at* www.uspto.gov/web/menu/utility.pdf. In that example, a cDNA

fragment disclosed as being useful as a probe to obtain the full length gene corresponding to a cDNA fragment was deemed to lack a specific and substantial utility. Additionally, the MPEP particularly explains that a claim directed to a polynucleotide disclosed to be useful as a "gene probe" or "chromosome marker," as is the case here, fails to satisfy the specific utility requirement unless a specific DNA target is also disclosed. Manual of Patent Examining Procedure § 2107.01.

Regarding the seven uses asserted by Fisher, we observe that each claimed EST uniquely corresponds to the single gene from which it was transcribed ("underlying gene"). As of the filing date of the '643 application, Fisher admits that the underlying genes have no known functions. Fisher, nevertheless, claims that this fact is irrelevant because the seven asserted uses are not related to the functions of the underlying genes. We are not convinced by this contention. Essentially, the claimed ESTs act as no more than research intermediates that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. The overall goal of such experimentation is presumably to understand the maize genome—the functions of the underlying genes, the identity of the encoded proteins, the role those proteins play during anthesis, whether polymorphisms exist, the identity of promoters that trigger protein expression, whether protein expression may be controlled, etc. Accordingly, the claimed ESTs are, in words of the Supreme Court, mere "object[s] of use-testing," to wit, objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end. *Brenner*, 383 U.S. at 535, 86 S.Ct. 1033.

Fisher compares the claimed ESTs to certain other patentable research tools, such as a microscope. Although this comparison may, on first blush, be appealing in that both a microscope and one of the claimed ESTs can be used to generate scientific data about a sample having unknown properties, Fisher's analogy is flawed. As the government points out, a microscope has the specific benefit of optically magnifying an object to immediately reveal its structure. One of the claimed ESTs, by contrast, can only be used to detect the presence of genetic material having the same structure as the EST itself. It is unable to provide any information about the overall structure let alone the function of the underlying gene. Accordingly, while a microscope can offer an immediate, real world benefit in a variety of applications, the same cannot be said for the claimed ESTs. Fisher's proposed analogy is thus inapt. Hence, we conclude that Fisher's asserted uses are insufficient to meet the standard for a "substantial" utility under § 101.

Moreover, all of Fisher's asserted uses represent merely hypothetical possibilities, objectives which the claimed ESTs, or any EST for that matter, *could* possibly achieve, but none for which they have been used in the real world. Focusing on the two uses emphasized by Fisher at oral argument, Fisher maintains that the claimed ESTs could be used to identify polymorphisms or to isolate promoters. Nevertheless, in the face of a utility rejection, Fisher has not presented any evidence, as the Board well noted, showing that the claimed ESTs have been used in either way. That is, Fisher does not present either a single polymorphism or a single promoter, assuming at least one of each exists, actually identified by using the claimed ESTs. Further, Fisher has not shown that a polymorphism or promoter so identified would have a "specific and substantial" use. The Board, in fact, correctly recognized this very deficiency and cited it

as one of the reasons for upholding the examiner's final rejection.

With respect to the remaining asserted uses, there is no disclosure in the specification showing that any of the claimed ESTs were used as a molecular marker on a map of the maize genome. There also is no disclosure establishing that any of the claimed ESTs were used or, for that matter, could be used to control or provide information about gene expression. Significantly, despite the fact that maize leaves produce over two thousand different proteins during anthesis, Fisher failed to show that one of the claimed ESTs translates into a portion of one of those proteins. Fisher likewise did not provide any evidence showing that the claimed ESTs were used to locate genetic molecules in other plants and organisms. What is more, Fisher has not proffered any evidence showing that any such generic molecules would themselves have a specific and substantial utility. Consequently, because Fisher failed to prove that its claimed ESTs can be successfully used in the seven ways disclosed in the '643 application, we have no choice but to conclude that the claimed ESTs do not have a "substantial" utility under § 101.

Furthermore, Fisher's seven asserted uses are plainly not "specific." Any EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses. That is, any EST transcribed from any gene in the maize genome may be a molecular marker or a source for primers. Likewise, any EST transcribed from any gene in the maize genome may be used to measure the level of mRNA in a tissue sample, identify the presence or absence of a polymorphism, isolate promoters, control protein expression, or locate genetic molecules of other plants and organisms. Nothing about Fisher's seven alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the '643 application or indeed from any EST derived from any organism. Accordingly, we conclude that Fisher has only disclosed general uses for its claimed ESTs, not specific ones that satisfy § 101.

We agree with the Board that the facts here are similar to those in *Brenner*. There, as noted above, the applicant claimed a process for preparing compounds of unknown use. Similarly, Fisher filed an application claiming five particular ESTs which are capable of hybridizing with underlying genes of unknown function found in the maize genome. The *Brenner* court held that the claimed process lacked a utility because it could be used only to produce a compound of unknown use. The *Brenner* court stated: "We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product." 383 U.S. at 535, 86 S.Ct. 1033. Applying that same logic here, we conclude that the claimed ESTs, which do not correlate to an underlying gene of known function, fail to meet the standard for utility intended by Congress.

In addition to approving of the Board's reliance on *Brenner*, we observe that the facts here are even more analogous to those presented in *Kirk*, 54 C.C.P.A. 1119, 376 F.2d 936, and *In re Joly*, 54 C.C.P.A. 1159, 376 F.2d 906 (1967), two cases decided by our predecessor court shortly after *Brenner*. In *Kirk*, the applicant sought to patent new steroidal compounds disclosed as having two possible utilities. First, the applicant alleged that the claimed compounds were useful for their "biological activity" because "one skilled in the art would know how to use the compounds . . .

to take advantage of their presently-existing biological activity." *Kirk*, 376 F.2d at 939. The court rejected this claimed utility on the ground that it was not sufficiently "specific," but was instead "nebulous." *Id.* at 941.

Second, the applicant asserted that the claimed compounds could be used by skilled chemists as intermediates in the preparation of final steroidal compounds of unknown use. Relying on *Brenner*, the court reasoned:

> It seems clear that, if a process for producing a product of only conjectural use is not itself "useful" within § 101, it cannot be said that the starting materials for such a process—*i.e.*, the presently claimed intermediates—are "useful." It is not enough that the specification disclose that the intermediate exists and that it "works," reacts, or can be used to produce some intended product of no known use. Nor is it enough that the product disclosed to be obtained from the intermediate belongs to some class of compounds which now is, or in the future might be, the subject of research to determine some *specific use*. *Cf. Reiners v. Mehltretter*, 43 C.C.P.A. 1019, 236 F.2d 418, 421 [(C.C.P.A.1956)] where compounds employed as intermediates to produce other directly useful compounds were found to be themselves useful.

Id. at 945–46 (emphasis added). Therefore, the court affirmed the Board's rejection of the claimed compounds for lack of utility.

The facts in *Joly* are nearly identical to the facts in *Kirk*. The *Joly* applicant filed an application claiming compounds useful as intermediates in preparing steroids that were themselves not shown or known to be useful, but that were similar in chemical structure to steroids of known pharmacological usefulness. The court adopted the reasoning of the *Kirk* court in its entirety and affirmed the Board's decision rejecting the claimed intermediates for failing to comply with § 101. *Joly*, 376 F.2d at 908–09.

Just as the claimed compounds in *Kirk* and *Joly* were useful only as intermediates in the synthesis of other compounds of unknown use, the claimed ESTs can only be used as research intermediates in the identification of underlying protein-encoding genes of unknown function. The rationale of *Kirk* and *Joly* thus applies here. In the words of the *Kirk* court:

> We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound *in terms of possible use so general as to be meaningless* and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.

376 F.2d at 942 (emphasis added).

That the *Kirk* and *Joly* decisions involved chemical compounds, while the present case involves biological entities, does not distinguish these decisions. The rationale presented therein, having been drawn from principles set forth by the Supreme Court in *Brenner*, applies with equal force in the fields of chemistry and biology as well as in any scientific discipline. In *Brenner*, the Supreme Court was primarily concerned with creating an unwarranted monopoly to the detriment of the public:

> Whatever weight is attached to the value of encouraging disclosure and of inhibiting secrecy, we believe a more compel-

> ling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development, without compensating benefit to the public.... This is not to say that we mean to disparage the importance of contributions to the fund of scientific information short of the invention of something "useful," or that we are blind to the prospect that what now seems without "use" may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. [A] patent system must be related to the world of commerce rather than to the realm of philosophy.

Brenner, 383 U.S. at 535–36, 86 S.Ct. 1033 (citations, quotation, and footnote omitted). Here, granting a patent to Fisher for its five claimed ESTs would amount to a hunting license because the claimed ESTs can be used only to gain further information about the underlying genes and the proteins encoded for by those genes. The claimed ESTs themselves are not an end of Fisher's research effort, but only tools to be used along the way in the search for a practical utility. Thus, while Fisher's claimed ESTs may add a noteworthy contribution to biotechnology research, our precedent dictates that the '643 application does not meet the utility requirement of § 101 because Fisher does not identify the function for the underlying protein-encoding genes. Absent such identification, we hold that the claimed ESTs have not been researched and understood to the point of providing an immediate, well-defined, real world benefit to the public meriting the grant of a patent.

2.

Fisher's reliance on *Jolles*, *Nelson*, and *Cross*, cases which found utility in certain claimed pharmaceutical compounds, is misplaced. In *Jolles*, the applicant filed an application claiming naphthacene compounds useful in treating acute myloblastic leukemia. To support the asserted utility, the applicant presented *in vivo* data showing eight of the claimed compounds effectively treated tumors in a mouse model. Our predecessor court reversed the Board's affirmance of the final rejection for lack of utility, finding that the structural similarity between the compounds tested *in vivo* and the remaining claimed compounds was sufficient to establish utility for the remaining claimed compounds. *Jolles*, 628 F.2d at 1327–28.

In *Nelson*, decided by the Court of Customs and Patent Appeals in the same year as *Jolles*, Nelson claimed prostaglandin compounds. The PTO declared an interference with an application filed by Bowler claiming the same compounds. The issue before the Board was whether Nelson had established utility for the claimed prostaglandins as smooth muscle stimulants and blood pressure modulators via *in vivo* and *in vitro* data, specifically, an *in vivo* rat blood pressure test and an *in vitro* gerbil colon smooth muscle stimulation test. The Board declined to award priority to Nelson, characterizing Nelson's tests as "rough screens, uncorrelated with actual utility [in humans]." Our predecessor court reversed, concluding that "tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use." *Nelson*, 626 F.2d at 856.

In *Cross*, decided by the Federal Circuit five years after *Jolles* and *Nelson*, Iizuka filed an application claiming thromboxane synthetase inhibitors, alleged to be useful in treating inflammation, asthma, hypertension, and other ailments. When Cross filed an application claiming the same compounds two months after Iizuka, the PTO declared an interference. The dispositive issue concerned whether Iizuka's Japanese priority application disclosed utility for the claimed inhibitors. The Board concluded that it offered a sufficient disclosure based upon *in vitro* data showing strong inhibitory action for thromboxane synthetase for structurally-similar compounds in human or bovine platelet microsomes. We affirmed, reasoning:

> Opinions of our predecessor court have recognized the fact that pharmacological testing of animals is a screening procedure for testing new drugs for practical utility. This *in vivo* testing is but an intermediate link in a screening chain which may eventually lead to the use of the drug as a therapeutic agent in humans. We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility.

Cross, 753 F.2d at 1050 (citations omitted).

The facts in these three cases are readily distinguishable from the facts here. In *Jolles*, *Nelson*, and *Cross*, the applicants disclosed specific pharmaceutical uses in humans for the claimed compounds and supported those uses with specific animal test data, *in vitro*, *in vivo*, or both. In contrast, Fisher disclosed a variety of asserted uses for the claimed ESTs, but failed to present any evidence—test data, declaration, deposition testimony, or otherwise—to support those uses as presently beneficial and hence practical. Fisher did not show that even one of the claimed ESTs had been tested and successfully aided in identifying a polymorphism in the maize genome or in isolating a single promoter that could give clues about protein expression. Adopting the language of the *Cross* court, the alleged uses in *Jolles*, *Nelson*, and *Cross* were not "nebulous expressions, such as 'biological activity' or 'biological properties' [alleged in the application in *Kirk*]," that "convey little explicit indication regarding the utility of a compound." *Cross*, 753 F.2d at 1048. Instead, the alleged uses in those cases gave a firm indication of the precise uses to which the claimed compounds could be put. For example, in *Nelson*, the claimed prostaglandins could be used to stimulate smooth muscle or modulate blood pressure in humans as shown by both *in vivo* and *in vitro* animal data. Hence, the *Jolles*, *Nelson*, and *Cross* courts concluded that the claimed pharmaceutical compounds satisfied the specific and substantial utility requirements of § 101. We cannot reach that same conclusion here. Fisher's laundry list of uses, like the terms "biological activity" or "biological properties" alleged in *Kirk*, are nebulous, especially in the absence of any data demonstrating that the claimed ESTs were actually put to the alleged uses.

Fisher's reliance on the commercial success of general EST databases is also misplaced because such general reliance does not relate to the ESTs at issue in this case. Fisher did not present any evidence showing that agricultural companies have purchased or even expressed any interest in the claimed ESTs. And, it is entirely unclear from the record whether such business entities ever will. Accordingly, while

commercial success may support the utility of an invention, it does not do so in this case. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 959 (Fed.Cir.1983) (stating that proof of a utility may be supported when a claimed invention meets with commercial success).

3.

As a final matter, we observe that the government and its amici express concern that allowing EST patents without proof of utility would discourage research, delay scientific discovery, and thwart progress in the "useful Arts" and "Science." *See* U.S. Const. art. I, § 8, cl. 8. The government and its amici point out that allowing EST claims like Fisher's would give rise to multiple patents, likely owned by several different companies, relating to the same underlying gene and expressed protein. Such a situation, the government and amici predict, would result in an unnecessarily convoluted licensing environment for those interested in researching that gene and/or protein.

The concerns of the government and amici, which may or may not be valid, are not ones that should be considered in deciding whether the application for the claimed ESTs meets the utility requirement of § 101. The same may be said for the resource and managerial problems that the PTO potentially would face if applicants present the PTO with an onslaught of patent applications directed to particular ESTs. Congress did not intend for these practical implications to affect the determination of whether an invention satisfies the requirements set forth in 35 U.S.C. §§ 101, 102, 103, and 112. They are public policy considerations which are more appropriately directed to Congress as the legislative branch of government, rather than this court as a judicial body responsible simply for interpreting and applying statutory law. Under Title 35, an applicant is entitled to a patent if his invention is new, useful, nonobvious, and his application adequately describes the claimed invention, teaches others how to make and use the claimed invention, and discloses the best mode for practicing the claimed invention. What is more, when Congress enacted § 101, it indicated that "anything under the sun that is made by man" constitutes potential subject matter for a patent. S.Rep. No. 82–1979, at 7 (1952), U.S.Code Cong. & Admin.News at 2394, 2399. Policy reasons aside, because we conclude that the utility requirement of § 101 is not met, we hold that Fisher is not entitled to a patent for the five claimed ESTs.

B. Enablement

[5] Fisher asserts that we should reverse the enablement rejection upheld by the Board since the Board made it contingent upon the utility rejection, which Fisher argues was not supported by substantial evidence for reasons analyzed above. The government argues to the contrary, asserting that claim 1 of the '643 application cannot be enabled because the claimed ESTs were not disclosed as having a specific and substantial utility. We agree with the government. It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101.

> The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112.

Ziegler, 992 F.2d at 1200–01 (citations omitted); *see also Kirk*, 376 F.2d at 942 ("Necessarily, compliance with § 112 re-

quires a description of how to use presently useful inventions, otherwise an applicant would anomalously be required to teach how to use a useless invention."); *In re Brana*, 51 F.3d 1560, 1564 (Fed.Cir.1995) ("Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it."); Manual of Patent Examining Procedure § 2107.01. Here, in light of our conclusion that the Board's decision with respect to utility applied the correct legal standard and was supported by substantial evidence, we conclude that Fisher failed to satisfy the enablement requirement. Consequently, we leave undisturbed the enablement rejection of the '643 application under § 112, first paragraph.

III. CONCLUSION

We conclude that substantial evidence supports the Board's findings that each of the five claimed ESTs lacksa specific and substantial utility and that they are not enabled. Accordingly, the Board's decision affirming the final rejection of claim 1 of the '643 patent for lack of utility under § 101 and lack of enablement under § 112, first paragraph, is affirmed.

AFFIRMED.

RADER, Circuit Judge, dissenting.

This court today determines that expressed sequence tags (ESTs) do not satisfy 35 U.S.C. § 101 unless there is a known use for the genes from which each EST is transcribed. While I agree that an invention must demonstrate utility to satisfy § 101, these claimed ESTs have such a utility, at least as research tools in isolating and studying other molecules. Therefore, I respectfully dissent.

Several, if not all, of Fisher's asserted utilities claim that ESTs function to study other molecules. In simple terms, ESTs are research tools. Admittedly ESTs have use only in a research setting. However, the value and utility of research tools generally is beyond question, even though limited to a laboratory setting. *See* U.S. Pat. & Trademark Off., Manual of Patent Examining Procedure (MPEP) § 2107.01 at 2100–33 (8th ed.2001, rev.Feb.2003) ("Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds)."). Thus, if the claimed ESTs qualify as research tools, then they have a "specific" and "substantial" utility sufficient for § 101. If these ESTs do not enhance research, then *Brenner v. Manson*, 383 U.S. 519, 86 S.Ct. 1033, 16 L.Ed.2d 69 (1966) (involving the patentability of methods for producing compounds having no known use) controls and erects a § 101 bar for lack of utility. For the following reasons, these claimed ESTs are more akin to patentable research tools than to the unpatentable methods in *Brenner*.

In *Brenner*, the Court confronted a growing conflict between this court's predecessor, the Court of Customs and Patent Appeals (CCPA), and the Patent Office over the patentability of methods of producing compounds with no known use. This conflict began with *In re Nelson*, 47 C.C.P.A. 1031, 280 F.2d 172 (1960), the first in a series of cases wherein the CCPA reversed several Patent Office utility rejections. *Brenner*, 383 U.S. at 530, 86 S.Ct. 1033. *Brenner* put an end to these cases because, in the 1960s, the Court could not distinguish between denying patents to compounds with no known use and denying patents to methods of producing those useless compounds. The Court commented:

> We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing, a different set of rules

> was meant to apply to the process which yielded the unpatentable product. That proposition seems to us little more than an attempt to evade the impact of the rules which concededly govern patentability of the product itself.

Id. at 535, 86 S.Ct. 1033. This court's predecessor later extended *Brenner* to bar patents on compounds as intermediates in the preparation of other compounds having no known use. *See In re Kirk*, 54 C.C.P.A. 1119, 376 F.2d 936 (1967) (rejecting intermediaries for steroids with no known use). These cases, however, share a common underpinning—a method of producing a compound with no known use has no more benefit to society than the useless compound itself.

This case is very different. Unlike the methods and compounds in *Brenner* and *Kirk*, Fisher's claimed EST's *are* beneficial to society. As an example, these research tools "may help scientists to isolate the particular underlying protein-encoding genes... [with the] overall goal of such experimentation ... presumably [being] to understand the maize genome[.]" *Majority Opinion*, at 1373. They also can serve as a probe introduced into a sample tissue to confirm "that the gene corresponding to the EST was being expressed in the sample tissue at the time of mRNA extraction." *Id.*, at 1367.

These research tools are similar to a microscope; both take a researcher one step closer to identifying and understanding a previously unknown and invisible structure. Both supply information about a molecular structure. Both advance research and bring scientists closer to unlocking the secrets of the corn genome to provide better food production for the hungry world. If a microscope has § 101 utility, so too do these ESTs.

The Board and this court acknowledge that the ESTs perform a function, that they have a utility, but proceed quickly to a value judgment that the utility would not produce enough valuable information. The Board instead complains that the information these ESTs supply is too "insubstantial" to merit protection. Yet this conclusion denies the very nature of scientific advance. Science always advances in small incremental steps. While acknowledging the patentability of research tools generally (and microscopes as one example thereof), this court concludes with little scientific foundation that these ESTs do not qualify as research tools because they do not "offer an immediate, real world benefit" because further research is required to understand the underlying gene. This court further faults the EST research for lacking any "assurance that anything useful will be discovered in the end." These criticisms would foreclose much scientific research and many vital research tools. Often scientists embark on research with no assurance of success and knowing that even success will demand "significant additional research."

Nonetheless, this court, oblivious to the challenges of complex research, discounts these ESTs because it concludes (without scientific evidence) that they do not supply enough information. This court reasons that a research tool has a "specific" and "substantial" utility *only* if the studied object is readily understandable using the claimed tool—that no further research is required. Surely this cannot be the law. Otherwise, only the final step of a lengthy incremental research inquiry gets protection.

Even with a microscope, significant additional research is often required to ascertain the particular function of a "revealed" structure. To illustrate, a cancerous growth, magnified with a patented microscope, can be identified and distinguished from other healthy cells by a properly trained doctor or researcher. But even today, the scientific community

still does not fully grasp the reasons that cancerous growths increase in mass and spread throughout the body,[1] or the nature of compounds that interact with them, or the interactions of environmental or genetic conditions that contribute to developing cancer. Significant additional research is required to answer these questions. Even with answers to these questions, the cure for cancer will remain in the distance. Yet the microscope still has "utility" under § 101. Why? Because it takes the researcher one step closer to answering these questions. Each step, even if small in isolation, is nonetheless a benefit to society sufficient to give a viable research tool "utility" under § 101. In fact, experiments that fail still serve to eliminate some possibilities and provide information to the research process.

The United States Patent Office, above all, should recognize the incremental nature of scientific endeavor. Yet, in the interest of easing its administrative load, the Patent Office will eliminate some research tools as providing "insubstantial" advances. How does the Patent Office know which "insubstantial" research step will contribute to a substantial breakthrough in genomic study? Quite simply, it does not.

In addition, this court faults Fisher for not presenting evidence of utility showing that the claimed ESTs "have been used in the real world." To the contrary, this court misapprehended the proper procedure. Fisher asserted seven different utilities. The Board rejected two of these assertions outright as "insubstantial." *See Ex parte Fisher*, App. No.2002–2046, slip. op at 14–16 (Bd. Pat.App. and Int.2004) (acknowledging that the ESTs may be able to detect "the absence of a polymorphism" and "to isolate nucleic acid molecules of other plants and organisms[,]" but finding such utilities are not "substantial" even if the ESTs can perform them). This summary dismissal deprived Fisher of any chance to proffer evidence. Rather than fault Fisher for not presenting evidence it was prevented from offering, this court should instead observe that the Board did not satisfy its burden of challenging Fisher's presumptively correct assertion that the ESTs were *capable* of performing those functions. *See* MPEP § 2107.02(IV) at 2100–40 (noting that the initial burden is on the office to establish a prima facie case as to lack of utility and to provide evidentiary support thereof); *In re Brana*, 51 F.3d 1560, 1566 (Fed.Cir.1995) (where an applicant has asserted utility in the disclosure, the Patent Office has the initial burden of challenging this presumptively correct assertion of utility).

Abandoning the proper legal procedure, the Board reasoned that the molecules studied with these ESTs showed no particular use, therefore the ESTs themselves also lacked a utility. In so ruling, the Board did not reject Fisher's utilities on the basis that the ESTs were *unable to perform* the purported utilities. Thus, the Board did not establish a prima facie challenge to the ESTs' ability to perform these two utilities. Without anything to rebut, Fisher had no obligation or opportunity to provide evidence in rebuttal. Thus, I respectfully disagree with this court's conclusion that the Board's decision can be affirmed on the basis that Fisher did not supply evidence of the ESTs' ability to perform the asserted utilities.

In truth, I have some sympathy with the Patent Office's dilemma. The Office needs

1. ESTs have already been used to advance cancer research well beyond what is achievable using microscopes alone. *See* Andy J. Minn, *Genes That Mediate Breast Cancer Metastisis To Lung*, Nature, July 28, 2005 at 518–24 (discussing research to identify genes that mark and mediate breast cancer metastisis to the lung).

some tool to reject inventions that may advance the "useful arts" but not sufficiently to warrant the valuable exclusive right of a patent. The Patent Office has seized upon this utility requirement to reject these research tools as contributing "insubstantially" to the advance of the useful arts. The utility requirement is ill suited to that task, however, because it lacks any standard for assessing the state of the prior art and the contributions of the claimed advance. The proper tool for assessing sufficient contribution to the useful arts is the obviousness requirement of 35 U.S.C. § 103. Unfortunately this court has deprived the Patent Office of the obviousness requirement for genomic inventions. *See In re Deuel*, 51 F.3d 1552 (Fed. Cir.1995); Martin J. Adelman et al., *Patent Law*, 517 (West Group 1998) (commenting that scholars have been critical of *Deuel*, which "overly favored patent applicants in biotech by adopting an overly lax nonobviousness standard." (*citing* Anita Varma & David Abraham, *DNA Is Different: Legal Obviousness and the Balance Between Biotech Inventors and the Market*, 9 Harv. J.L. & Tech. 53 (1996))); Philippe Ducor, *The Federal Circuit and In re Deuel: Does § 103 apply to Naturally Occurring DNA?*, 77 J. Pat. & Trademark Off. Soc'y 871, 883 (Nov.1995) ("The Court of Appeals for the Federal Circuit could have formulated its opinion in only one sentence: '35 U.S.C. § 103 does not apply to newly retrieved natural DNA sequences.' "); Philippe Ducor, *Recombinant Products and Nonobviousness: A Typology*, 13 Santa Clara Computer and High Tech. L.J. 1, 44–45 (Feb.1997) ("This amounts to a practical elimination of the requirement for nonobviousness for these products, even when all the information necessary to discover them is previously available."); *see also* over fifty additional articles critical of *Deuel* in the "Citing References" tab for *Deuel* on Westlaw. Nonetheless, rather than distort the utility test, the Patent Office should seek ways to apply the correct test, the test used world wide for such assessments (other than in the United States), namely inventive step or obviousness.

Thus, for the foregoing reasons, I would find that Fisher's asserted utilities qualify the claimed ESTs as research tools useful in the study of other molecules. Because research tools provide a cognizable benefit to society, much like a microscope, the ESTs claimed here have "utility" under § 101. In addition, the enablement rejection should also be reversed because it was a consequence of the finding of lack of utility.